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Substantial discrepancy between fluid and weight loss during acute decompensated heart failure treatment: Important lessons for research and clinical care

Jeffrey M. Testani, MD, MTR[1,2], **Meredith A. Brisco, MD, MSCE**[3], **Robb D. Kociol, MD**[3], **Daniel Jacoby, MD**[1], **Lavanya Bellumkonda, MD**[1], **Chirag R. Parikh, MD, PhD**[1,2], **Steven G. Coca, MD, MS**[1,2], and **W. H. Wilson Tang, MD**[5]

[1]Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut

[2]Program of Applied Translational Research, Yale University School of Medicine, New Haven, Connecticut

[3]Department of Medicine, Cardiovascular Division, Medical University of South Carolina, Charleston, South Carolina

[4]Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School

[5]Section of Heart Failure and Cardiac Transplantation, The Cleveland Clinic, Cleveland, Ohio

Abstract

Background—Net fluid and weight loss are ubiquitously employed to monitor diuretic response in acute decompensated heart failure research and patient care. However, the performance of these metrics has never been critically evaluated. The weight and volume of aqueous fluids such as urine should be nearly perfectly correlated and with very good agreement. As a result significant discrepancy between fluid and weight loss during the treatment of acute decompensated heart failure would indicate measurement error in one or both of the parameters.

Methods—The correlation and agreement (Bland-Altman method) between diuretic-induced fluid/weight loss were examined in three acute decompensated heart failure trials and cohorts: 1) DOSE (n=254) 2) ESCAPE (n=348) the 3) Penn (n=486).

Results—The correlation between fluid and weight loss was modest (DOSE r=0.55; ESCAPE r=0.48; Penn r=0.51; p<0.001 for all) and the 95% limits of agreement were wide (DOSE −7.9 to 6.4 Kg-L; ESCAPE −11.6 to 7.5 Kg-L; Penn −14.5 to 11.3 Kg-L). The median relative disagreement ranged from ± 47.0% to 63.5%. A bias toward greater fluid than weight loss was found across populations (−0.74 to −2.1 Kg-L p≤0.002). A consistent pattern of baseline

Address for correspondence: Jeffrey M. Testani, M.D., M.T.R., Yale University School of Medicine, 60 Temple Street, Suite 6C, New Haven, CT 06510, Tel: (215) 459-3709, Fax: (203) 746-8373, jeffrey.testani@yale.edu.

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characteristics or in-hospital treatment parameters that could identify patients at risk of discordant fluid and weight loss was not found.

Conclusions—Considerable discrepancy between fluid balance and weight loss is common in patients treated for acute decompensated heart failure. Awareness of the limitations inherent to these commonly used metrics and efforts to develop more reliable measures of diuresis are critical for both patient care and research in acute decompensated heart failure.

Keywords

Decompensated heart failure; diuretics; weight loss; net fluid output

Introduction

One of the primary objectives in the treatment of acute decompensated heart failure is relief of congestion. Although limited data are available to inform the optimal method for monitoring decongestion in acute decompensated heart failure, serial weight and fluid loss are measures extensively employed in clinical care and research, and use of these metrics is endorsed by cardiovascular society guidelines.[1–3] However, in practice it is widely acknowledged that net fluid output and serial changes in weight are difficult to obtain accurately.[2,4,5]

Given that decongestion of acute decompensated heart failure patients is one of the most common reasons for hospitalization and fluid/weight loss are ubiquitously used in both research and clinical care to monitor diuretic response, a better understanding of the performance of these parameters is critical. The objectives of this manuscript were the following; 1) Further explore the relationship between net fluid output and weight loss including assessment of agreement, bias, and patient/treatment related factors predicting lack of agreement. 2) Evaluate if discrepancy between fluid and weight loss influences discharge markers of decongestion and carries prognostic importance. Given that local practice patterns and fidelity of data collection can vary between different clinical and research populations, our objective was to explore these associations across multiple different settings to evaluate the consistency and generalizability of these findings.

Methods

The relationship between fluid and weight loss was explored in the 1) Diuretic Optimization Strategies Evaluation (DOSE) trial dataset, 2) Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial dataset and 3) the Penn acute decompensated heart failure clinical cohort. Given that DOSE was a contemporary trial of decongestive strategies; the primary analyses were undertaken in DOSE with ESCAPE and Penn acute decompensated heart failure primarily used for validation. Inclusion in this analysis required administration of intravenous loop diuretics to ensure active diuresis was a goal of the treatment team and availability of data on fluid and weight loss. Additional detail on each cohort can be found below.

DOSE Trial

The DOSE trial was a multicenter, randomized, double-blind, placebo controlled trial of diuretic strategies in patients with acute decompensated heart failure. The study design and results of have been previously published.[6,7] The study used a 2×2 factorial design randomizing patients to a strategy of high- vs. low-dose furosemide treatment and continuous infusion vs. bolus furosemide administration. Eligibility criteria included an oral loop diuretic dose 80–240 mg of furosemide equivalents. The randomized intervention was continued for 72 hours and the primary ascertainment of fluid and weight loss occurred over this interval. In cases where the length of stay was less than 72 hours, the 48 hour fluid or weight loss was used to calculate the change.

ESCAPE Trial

The ESCAPE Trial was a randomized, multicenter trial of therapy guided by pulmonary artery catheter vs. clinical assessment in hospitalized patients with acute decompensated heart failure. Methods and results have been published previously.[8,9] Inclusion criteria included treatment with more than 160 mg of furosemide equivalents daily and at least 1 sign and 1 symptom of congestion. Net fluid output and change in body weight were ascertained from randomization to discharge. Patients in the ESCAPE population that did not have data available to calculate net urine output (n=19) and patients that did not receive IV loop diuretics (n=24) were excluded from the analysis. Additional details of the assembly and characteristics of this subgroup of the ESCAPE trial have been previously published.[10]

Penn Cohort

Consecutive charts of patients with a primary discharge diagnosis of congestive heart failure who were admitted to non-interventional cardiology and internal medicine services at the Hospital of the University of Pennsylvania from 2004 to 2009 were reviewed. Briefly, inclusion required a B-type natriuretic peptide (BNP) level of > 100 pg/mL within 24 hours of admission, receipt of intravenous loop diuretics, and availability of data on fluid intake and output during the hospitalization. Additional details on the assembly of this cohort, including a consort diagram, have been previously published.[10] Net fluid output and change in body weight were ascertained between baseline and discharge.

Given that the correlation between fluid and weight loss appear to be limited (when it should approach unity) and available data does not support either fluid or weight loss as the primary source of this error; the average of fluid and weight loss were taken when a reference was required (i.e., Bland-Altman plots) and expressed as Kg-L. In all cohorts estimated glomerular filtration rate (eGFR) was determined using the Chronic Kidney Disease Epidemiology collaboration equation.[11] When the data was available, change in markers of hemoconcentration (hemoglobin, hematocrit, albumin, and total protein) were evaluated as the relative change in each marker from baseline to discharge. The study was approved by the Yale University Institutional Review Board.

Statistical methods

The primary analytic goals were to determine the correlation, agreement, and bias between fluid and weight loss across several heart failure populations and determine patient or

treatment parameters that were associated with disagreement. As a result, the primary outcomes of this analysis were the correlation coefficients and the bias and 95% limits of agreement using the methodology described by Bland and Altman.[12,13] Values reported are mean ± SD, median (quartile 1 – quartile 4) and percentile. Independent Student's *t* test, the Wilcoxon Rank Sum test, or the Mann Whitney U tests were used to compare continuous variables between groups of patients. The chi-square test was used to evaluate associations between categorical variables. Although previous investigation from the DOSE trial reported Pearson correlations, Spearman's rho was utilized in this analysis to minimize the effect of outliers which are common with fluid and weight loss. Bland-Altman Plots were constructed by plotting the difference between fluid and weight loss on the X axis and the average of fluid and weight loss on the Y axis. To allow easy visual comparison of the plots between cohorts, the range of the X axis was set at 7.5 times the mean of the average of fluid and weight loss and the Y axis was set at the 1st and 99th percentile of the average of fluid and weight loss. Bias was calculated as the mean of the difference between fluid and weight loss and the 95% limits of agreement were plotted at 1.96 times the standard deviation of the bias. The hypothesis that the bias was different than zero was tested using a one sample *t* test. Proportionality of the bias across the spectrum of different average fluid/weight loss was evaluated using Spearman's rho. Proportional hazards modeling was used to evaluate time-to-event associations with 1) death, rehospitalization, or emergency room visits (DOSE) 2) death or rehospitalization (ESCAPE) or 3) death (Penn). Candidate covariates entered in the model were all baseline, or in-hospital, or discharge characteristics that differed between groups of patients with discordant fluid and weight loss with a $p \leq 0.2$ (i.e., Table 1 and 3 in DOSE). Statistical analysis was performed with IBM SPSS Statistics version 19.0 (IBM Corp., Armonk, NY) and statistical significance was defined as a 2-tailed $p<0.05$.

Results

DOSE Trial

Baseline characteristics of the analyzed cohort are presented in Table 1. Overall 17.5% of the DOSE population was missing either fluid or weight loss over the 72 hour intervention period (Table 2). Amongst these patients, the correlation between net fluid and weight loss was modest (Table 2). The correlation tended to be worse on individual treatment days and decline further as the hospitalization progressed (Table 3). Agreement between the two metrics was poor with the 95% limits of agreement spanning 3.8 times the average fluid/weight loss of the population (Table 2, Figure 1A). There was a bias toward greater fluid than weight loss and this bias was largely constant across different degrees of fluid and weight loss (Table 2, Figure 1A).

Baseline characteristics, in-hospital treatment and outcome parameters, and discharge parameters were largely similar between categories of patients' fluid and weight loss within ± 50%, 50% greater fluid than weight loss, and 50% greater weight than fluid loss (Tables 1 & 4). There was a small but statistically significant difference in the change in blood urea nitrogen with a greater worsening in patients with significantly greater weight than fluid loss (Table 4). In patients with >50% higher weight than fluid loss, the net fluid intake was

similar, however the ratio of fluid intake to output was significantly higher (Table 4). On univariate analysis the rate of death, rehospitalization, or emergency room visits did not differ significantly between the groups (p=0.062) but outcomes were significantly worse in patients with fluid>weight loss compared to patients with similar fluid and weight loss (HR=1.5, 95% CI=1.0–2.2, p=0.041). However, this relationship was no longer significant after adjustment for baseline and in-hospital characteristics (HR=1.3, 95% CI 0.8–2.1, p=0.25). Serial measures of hemoconcentration were not available in the DOSE trial dataset.

Validation in the ESCAPE and Penn Cohorts

Data on change in weight and fluid status were missing in a similar proportion of the ESCAPE trial, but significantly greater percentage of the observational Penn cohort (Table 2). Overall, findings were similar to DOSE with a modest correlation between fluid and weight loss, wide 95% limits of agreement, large relative disagreement, and a bias toward greater fluid than weight loss (Table 2). The correlation between measures of hemoconcentration and fluid and weight loss was higher for change in weight than fluid loss, particularly for change in albumin and total protein (Table 5).

A greater number of differences between patients with relative disagreement between fluid and weight loss was found in ESCAPE and particularly in the observational Penn cohort where fluid and weight losses were not ascertained as part of a research protocol (Supplementary Tables 1–4). In both cohorts the general trend emerged for greater baseline congestion in the group with agreement between fluid and weight loss, more intense in-hospital treatment, but at the time of discharge measures of adequacy of decongestion were either not different across groups or superior in the groups with concordant information on fluid and weight loss (Supplementary Tables 1–4). Many of these differences appeared to be driven by the group with greater weight than fluid loss (Supplementary Tables 1–4).

The incidence of death or rehospitalization in the ESCAPE cohort was not different between groups with greater or less than 50% discrepancy in fluid and weight loss (adjusted p=0.56). However, in the Penn cohort, the risk of death was significantly different between groups (adjusted p=0.023) which was primarily driven by worse outcomes in patients with 50% greater weight than fluid loss (adjusted HR=1.5, 95% CI 1.0 to 2.2, p=0.036).

Discussion

The principal finding of this analysis is that the correlation and agreement between net fluid balance and weight loss in the setting of treatment for acute decompensated heart failure is substantially lower than expected. It is widely acknowledged by clinicians that care for heart failure patients that it is challenging to obtain accurate data on fluid and weight loss. Although it is impossible to determine from this analysis how much of this discrepancy is driven by fluid vs. weight loss, in all likelihood it is both. The limitations to ascertainment of accurate net fluid balances are well known and consist of factors such as unrecorded intake, episodes of incontinence, lack of adherence with urine collection by patients/staff, insensible losses, unaccounted stool, and fluid consumed in the form of food (i.e., fruit). However, daily weights are also challenging to obtain accurately. This error takes the form of not weighing patients on the same scale, weighing different times in the day and/or in relation to

meals/urination/defecation, use of bed scales, and different clothing or devices (i.e., telemetry boxes) between weighing. Given the large number of potential sources of error, it is not surprising that such large discrepancies were evident across the cohorts. Furthermore, in each patient the predominant factor causing inaccuracy is likely different. Given that identifying the source of error is often times not straightforward, and the fact that it is challenging even in expert hands to monitor day to day diuretic progress with improvement in symptoms or physical examination findings, our inability to accurately monitor diuretic progress is a major problem.

The implications of these findings for clinical practice are relatively straight-forward; clinicians should be cognizant of the limitations inherent to fluid and weight loss and strive to diligently obtain both parameters then evaluate on a case by case basis how to apply the data toward treatment decisions in individual patients. The ramifications of these findings for clinical trial endpoints present more of a challenge. The limited correlation/agreement between fluid and weight loss, parameters which essentially are measuring the same signal, indicates that one or both of the metrics is incorrect in a substantial percentage of cases. Notably, the 95% limits of agreement spanned a ~4–5 fold larger amount of fluid/weight loss than the average fluid/weight loss of the inpatient acute decompensated heart failure populations. In addition to the fact that it is obviously unacceptable for a clinical trial endpoint not to accurately measure the signal of interest, the increased signal to noise ratio introduced by the error inherent to these metrics will substantially increase the required sample size for these studies. Furthermore, it is plausible that various acute decompensated heart failure interventions could differentially influence fluid vs. weight loss. For example, tolvaptan is known to increase thirst potentially leading to underestimation of fluid intake thus biasing towards a greater recorded net fluid loss.[14]

As we move forward toward better defining optimal metrics of diuresis and decongestion, an important consideration is that the majority of the available surrogates for diuresis/decongestion all measure slightly different aspects of physiology. Importantly, many of these metrics can be considered more as exposure variables than true endpoints. For example, a weight loss of 5 lbs per day for 4 days may represent either significant under or over treatment if we knew them to be 50 lbs vs. 15 lbs volume overloaded respectively. However, in both sceneries, 5 lbs per day may have represented an ideal diuresis on hospital day 1. Moreover, due to the complex physiology of body fluid homeostasis, parameters such as hemoconcentration and cardiac filling pressures represent only a snapshot in time of one dimension of volume overload.[15] For example, a patient with acute myocardial infarction can be euvolemic but with a massively elevated pulmonary capillary wedge pressure whereas a critically ill patient with sepsis can have massive volume overload but low cardiac filling pressures and blood volume. Furthermore, both blood volume and filling pressures will be only transiently improved if significant extravascular volume overload has not yet equilibrated. As such, an ideal marker of true euvolemia will need to incorporate multiple parameters which describe physiology such as blood volume, filling pressures, extra cellular fluid volume, plasma refill rate, and arterial and venous tone. Furthermore, it will be important in planning and interpreting clinical trials to be cognizant if the strategy being tested is to improve the rate/safety of the exposure (i.e., rate of fluid removal, rapidity with which symptoms are improved, or lack of increase in creatinine at a specific time point) or

the very different endpoint of bringing a patient to true euvolemia. While we do not know whether it is a biological or a logistical variability in fluid and weight loss driving the discrepancy observed in this study, the true challenge will be not to gauge treatment success on the degree of change but rather to the ultimate target of euvolemia.

Limitations

The data sources for this study consisted of post-hoc analysis of clinical trial populations and a retrospective chart review of a single center of hospitalized acute decompensated heart failure patients. Although the fact that three distinct populations were used with relatively consistent results across the cohorts, the degree of generalizability of these findings to the general heart failure population is unclear. However, given that the populations consisted of clinical trials of acute decompensated heart failure or patients at tertiary care centers with dedicated heart failure programs, results are unlikely to be substantially better in general practice. The current data present correlation and relative agreement between the metrics. However, with the available data and lack of gold standard it is impossible to determine exactly where the errors are coming from and which metric is superior.

Conclusion

Despite essentially measuring the same signal, fluid and weight loss commonly have limited correlation and agreement to clinically significant degrees. Clinicians and researchers alike should be cognizant of the substantial limitations inherent to fluid and weight loss when caring for patients or designing clinical trials of decongestive therapies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Clinical significance

- During the treatment of acute decompensated heart failure, fluid and weight loss appear to have surprisingly limited correlation and agreement
- This discrepancy was consistently found across 3 diverse heart failure populations, including a randomized clinical trial of loop diuretic therapy
- Patient and in-hospital treatment characteristics could not explain the disagreement between fluid and weight loss
- Awareness of these limitations is critical for both patient care and research

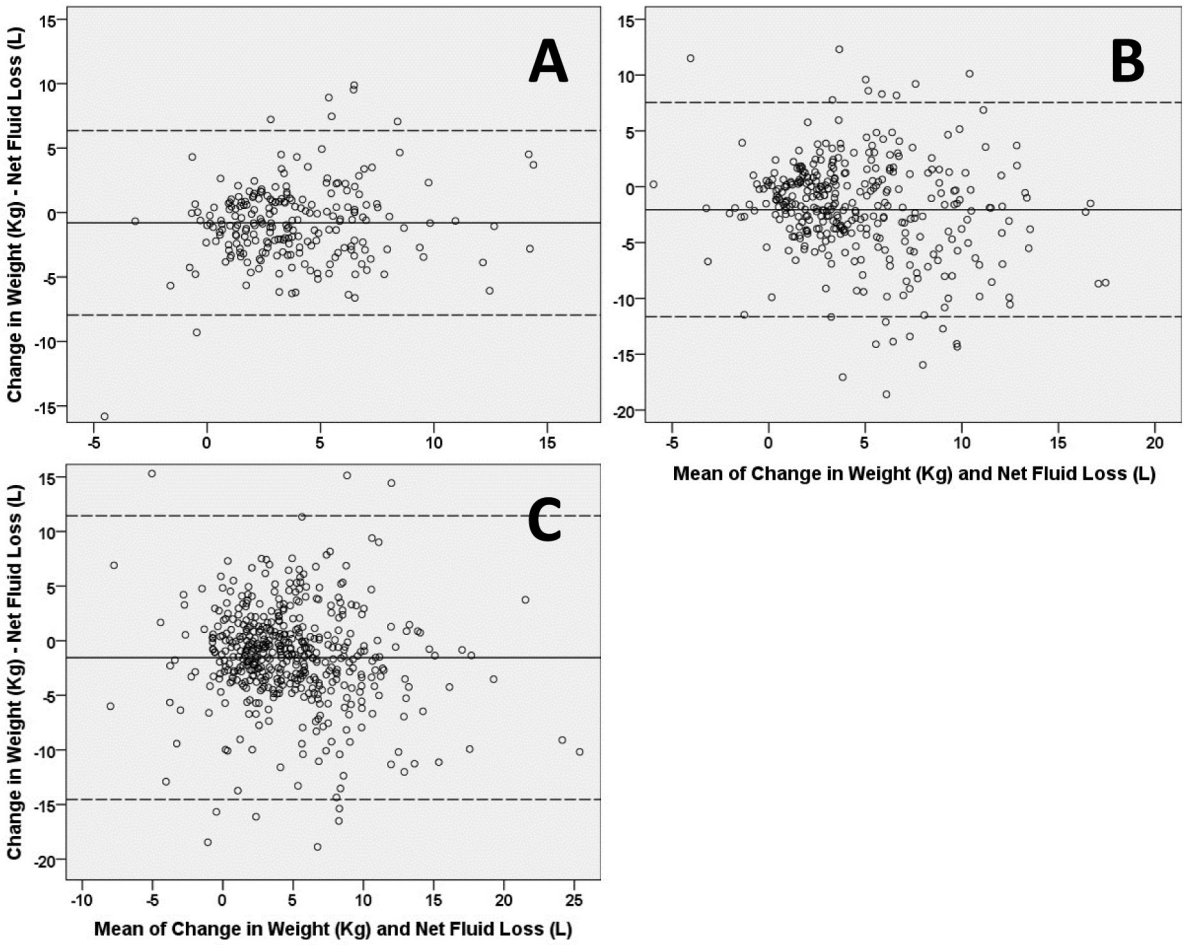

Figure 1. Bland-Altman plots of the agreement between fluid and weight loss in the studied HF populations

Panel **A**: DOSE trial; Panel **B** ESCAPE trial; Panel **C** Penn cohort. Solid lines represent the mean bias and dashed lines the 95 percent limits of agreement.

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Table 1

Baseline characteristics of the DOSE trial population stratified by relative agreement between fluid and weight loss

Characteristic	Overall cohort (n=254)	Fluid and weight loss within ± 50% (N=122)	Fluid ≥50% more than weight loss (N=84)	Weight ≥50% more than fluid loss (N=48)	p-value
Demographics					
Age (years)	67 ± 13.6	67 ± 14	66 ± 13	68 ± 14	0.594
Black race	20.1%	15.6%	27.4%	18.8%	0.338
Male	72.0%	74.6%	66.7%	75.0%	0.405
Medical History					
Hypertension	82.3%	92.8%	81.0%	83.3%	0.923
Diabetes	53.1%	50.8%	56.0%	54.2%	0.759
Ischemic heart disease	58.3%	57.4%	57.1%	62.5%	0.804
Ejection fraction ≥40%	34.1%	32.5%	33.7%	39.1%	0.719
Gout	24.8%	23.8%	23.8%	29.2%	0.739
Non-ischemic cardiomyopathy	50.0%	53.3%	48.8%	43.8%	0.516
Admission Physical Exam					
Weight (lbs)	217 ± 65	217 ± 61	218 ± 69	216 ± 68	0.855
Heart rate (beats/min)	78 ± 15	77 ± 17	76 ± 14	80 ± 14	0.424
Systolic blood pressure (mm Hg)	118 ± 19	118 ± 18	118 ± 20	117 ± 19	0.886
Jugular venous distention	63.0%	70.6%	57.0%	53.3%	0.050
Severe edema	32.7%	36.1%	32.1%	25.0%	0.380
Rales	59.5%	56.2%	60.7%	66.0%	0.494
S3	19.8%	18.6%	18.3%	25.5%	0.552
Randomized intervention					
Continuous infusion	47.6%	50.8%	40.5%	52.1%	0.272
High dose	51.6%	57.4%	45.2%	47.9%	0.197
Cardiac Function and Symptoms					
Ejection fraction (%)	35.1 ± 17.5	34.6 ± 17.9	35.4 ± 16.6	35.8 ± 18.2	0.851
NYHA Class	3.2 ± 0.6	3.3 ± 0.6	3.3 ± 0.5	3.2 ± 0.6	0.544
Laboratory Values					
Serum sodium (mEq/L)	138.2 ± 3.9	138.3 ± 3.8	138.0 ± 4.1	138.3 ± 3.6	0.797
NT-Pro BNP (pg/mL)	4490 (2443–11327)	4070 (2136–11472)	5178 (3073–11799)	5092 (2577–9882)	0.301

Characteristic	Overall cohort (n=254)	Fluid and weight loss within ± 50% (N=122)	Fluid ≥50% more than weight loss (N=84)	Weight ≥50% more than fluid loss (N=48)	p-value
eGFR (mL/min/1.73m^2)	52.8 ± 24.1	54.6 ± 24.8	49.0 ± 22.0	55.0 ± 25.4	0.251
Blood urea nitrogen (mg/dL)	38.8 ± 22.6	36.6 ± 21.8	42.3 ± 22.2	38.3 ± 25.2	0.078
Cystatin C (mg/L)	1.6 ± 0.6	1.6 ± 0.5	1.7 ± 0.6	1.6 ± 0.6	0.148
Hemoglobin (g/dL)	11.7 ± 2.0	11.9 ± 1.9	11.2 ± 2.0	11.9 ± 2.1	0.075
Uric Acid (mg/dl)	9.9 ± 2.6	9.8 ± 2.5	10.3 ± 2.7	9.3 ± 2.7	
Troponin (pg/ml)	43.2 ± 75.9	48.5 ± 96.3	33.1 ± 37.1	46.9 ± 65.5	
Renin (ng/ml/hr)	4.32 (0.8–16.0)	4.9 (0.9–15.7)	5.4 (0.8–20.9)	3.3 (0.7–14.2)	
Aldosterone (pg/ml)	215 (116–366)	186 (97–345)	245 (142–451)	225 (108–353)	
Medications (Admission)					
β-Blocker	83.5%	82.0%	86.9%	81.3%	
ACE inhibitor or ARB	60.6%	65.6%	50.0%	66.7%	
Digoxin	29.1%	24.6%	34.5%	31.3%	
Loop diuretic dose (mg)	120 (80–160)	120 (80–160)	120 (80–160)	120 (80–160)	
Aldosterone antagonist	29.9%	27.9%	27.4%	39.6%	

NTpro-BNP: N terminal pro B-type natriuretic peptide, eGFR: Estimated glomerular filtration rate. ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker.

*Significant p value.

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Table 2

Description of the correlation and agreement between fluid and weight loss across the different cohorts

	Trial/Cohort		
	DOSE	**ESCAPE**	**PENN**
Setting	Inpatient randomized trial of loop diuretic strategies in acute decompensated heart failure	Inpatient randomized trial of pulmonary artery catheters in acute decompensated heart failure	Inpatient retrospective observational acute decompensated heart failure cohort
Length of stay (days)	5 (3–9)	7 (5–10)	6 (4–9)
Diuretic observation period (days)*	3 (3–3)	7 (5–10)	6 (4–9)
Missing weight loss	12%	11%	26%
Missing net fluid loss	12%	4%	24%
IV loop diuretics not administered	0	6%	7%
N available for primary comparisons	254 (82.5%)	348 (80%)	486 (47%)
Mean weight loss (Kg)	3.4 ± 4.1	3.6 ± 4.7	4.1 ± 6.2
Mean net fluid loss (L)	4.2 ± 3.1	5.8 ± 5.2	5.2 ± 6.3
Correlation between net fluid and weight loss (r, p value)	r=0.55, p<0.001	r=0.48, p<0.001	r=0.51, p<0.001
95% limits of agreement (Kg-L)	−6.4 to 7.9	−7.5 to 11.6	−11.4 to 14.5
Ratio of 95% limits of agreement to average fluid-weight loss‡	3.8	4.1	5.4
Median relative disagreement (%)§	±47 (22.6–97.7)	±63.5 (23.4–120.6)	±51.7 (16.3–108.6)
Mean Bias (Kg-L)	−0.74 ± 3.8	−2.1 ± 4.9	−1.6 ± 6.6
p value different than zero	0.002	<0.001	<0.001
Proportionality of bias across values of fluid and weight loss (r, p value)	r=0.13, p=0.06	r=0.16, p=0.004	r=0.13, p=0.005

*Diuretic observation period indicates the period of time during which the fluid and weight loss were determined.

‡Calculated as the ratio of the span of the 95% limits of agreement divided by the mean of fluid and weight loss in the population.

§Calculated as the absolute value of the percentage difference between fluid and weight loss

Table 3

Correlation between fluid and weight loss on the individual days of hospitalization in the DOSE trial.

	n (%)	r	p
Baseline to 24 hours	283 (92)	0.47	<0.001
24 to 48 hours	267 (87)	0.47	<0.001
48 to 72 hours	233 (76)	0.30	<0.001
72 to 96 hours	194 (63)	0.23	0.001

N (%) represents the patients in the DOSE trial with data available during this interval.

Table 4

In-hospital and discharge characteristics of the DOSE trial population stratified by relative agreement between fluid and weight loss

Characteristic	Fluid and weight loss within ± 50% (N=122)	Fluid ≥50% more than weight loss (N=84)	Weight ≥50% more than fluid loss (N=48)	p-value
In hospital treatment				
Inotrope	11.5%	11.9%	12.5%	0.982
Vasodilator	8.2%	3.6%	8.3%	0.375
Thiazide diuretic	22.9%	16.3%	11.6%	0.229
Total study drug loop diuretic (mg) †	509 (310–829)	483 (288–735)	436 (226–733)	0.448
Total open label loop diuretic (mg)†	0 (0–53)	0 (0–75)	0 (0–125)	0.742
Total loop diuretic (mg)†	598 (383–892)	570 (325–870)	536 (340–766)	0.571
In hospital findings/outcomes				
Fluid intake (ml)†	4113 ± 1319	4270 ± 1430	4343 ± 1809	0.740
Fluid output (ml)†	9134 ± 3409	8474 ± 2772	5967 ± 2116	0.000*
Ratio of intake to output†	0.5 ± 0.2	0.6 ± 0.3	0.7 ± 0.2	0.000*
Net fluid output (ml)†	5021 ± 3221	4204 ± 2528	1624 ± 1503	0.000*
Weight loss (kg)†	4.9 ± 3.0	1.3 ± 1.5	3.1 ± 7.3	0.000*
Congestion free at 24 hours	3.3%	1.2%	2.1%	0.616
Congestion free at 48 hours	7.6%	6.0%	6.4%	0.905
Congestion free at 72 hours	13.0%	6.4%	14.6%	0.266
Patients' global assessment of symptoms†	4408 ± 1394	4166 ± 1510	4065 ± 1260	0.255
Treatment failure†	35.2%	40.5%	41.7%	0.644
Worsening or persistent HF	23.8%	29.8%	25.0%	0.619
Length of stay (days)	5 (3–9)	6 (4–9)	6 (3–10)	0.108
Change in laboratory parameters from randomization to 72 hours				
NTpro-BNP (pg/ml)	−674 (−2580 to 27)	−957 (−2836 to 264)	−994 (−2581 to −216)	0.847
Creatinine (mg/dl)	0.4 ± 0.3	0.0 ± 0.3	0.1 ± 0.3	0.166
Increase in creatinine ≥ 0.3 mg/dl	12.3%	17.9%	27.1%	0.066
Cystatin-C (mg/L)	0.1 ± 0.3	0.1 ± 0.4	0.2 ± 0.4	0.678
eGFR (ml/min/1.73m^2)	−2.2 ± 11.3	−1.1 ± 10.6	−3.1 ± 12.9	0.501
Blood urea nitrogen (mg/dL)	0.9 ± 10.1	3.2 ± 13.0	5.5 ± 9.1	0.022*
Serum sodium (mmol/L)	0.1 ± 3.2	0.3 ± 3.4	−1.0 ± 3.6	0.130
Medications (Discharge)				
β-Blocker	75.2%	86.7%	78.3%	0.129
ACE inhibitor or ARB	59.5%	59.0%	60.9%	0.979
Digoxin	32.2%	44.6%	30.4%	0.134
Thiazide diuretic	14.8%	12.3%	16.3%	0.814
Loop diuretic dose (mg)	160 (80–200)	160 (80–240)	160 (80–160)	0.546

Characteristic	Fluid and weight loss within ± 50% (N=122)	Fluid ≥50% more than weight loss (N=84)	Weight ≥50% more than fluid loss (N=48)	p-value
Aldosterone antagonist	35.5%	37.3%	32.7%	0.865
Discharge Physical Examination findings				
Heart rate (beats/min)	78 ± 16	76.5 ± 13.0	77.0 ±11.5	0.900
Systolic blood pressure (mmHg)	109 ± 15	112 ± 19	113 ± 17	0.629
Jugular venous distention	15.4%	16.0%	29.2%	0.305
Edema	42.6%	39.2%	19.6%	0.628

NTpro-BNP: N terminal pro B-type natriuretic peptide, eGFR: Estimated glomerular filtration rate. ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker.

† variable ascertained from randomization to 72 hours.

* Significant p value.

Table 5

Correlation of measures of hemoconcentration with fluid and weight loss

	% Change in Hematocrit		% Change in Hemoglobin		% Change in Albumin		% Change in Total Protein	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
ESCAPE[†]								
Net Fluid Output	0.133	0.022*	0.121	0.039*	0.158	0.058	0.171	0.052
Weight Change	0.140	0.021*	0.132	0.030*	0.231	0.006*	0.249	0.005*
PENN								
Net Fluid Output	0.108	0.008*	0.118	0.003*	--	--	--	--
Weight Change	0.235	<0.001*	0.219	<0.001*	--	--	--	--

[†]data on total protein and albumin were available in n=144 patients in the ESCAPE trial.

*Significant p value.